## CLAIMS

1. An isolated KOR-3 splice variant polypeptide comprising at least five consecutive amino acid residues thereof and retaining KOR-3 activity, where the KOR-3 polypeptides are not the same as any known polypeptides derived from a KOR-3 polypeptide.

2. The polypeptide according to claim 1, where the activity is selected from the group consisting of functional, immunologic, or pharmacological activity.

3. The immunologic activity according to claim 2, where the activity is binding to anti-opioid receptor antigen binding fragments selected from the group consisting of whole native antibodies, bispecific antibodies, chimeric antibodies, Fab, F(ab')2, single chain V region fragments (scFv), and fusion polypeptides comprising an antigen-binding fragment fused to a chemically functional moiety.

4. The pharmacologic activity according to claim 2, where the activity is activation or deactivation of the KOR-3 splice variant polypeptide upon binding of agonists and antagonists.

5. The polypeptide according to claim 1, where the KOR-3 polypeptide comprises mouse KOR-3A as depicted in Figure 2.

6. The polypeptide according to claim 5, where the KOR-3 polypeptide comprises amino acids encoded by exon 1a.

7. The polypeptide according to claim 1, where the KOR-3 polypeptide comprises mouse KOR-3B as depicted in Figure 3.

8. The polypeptide according to claim 7, where the KOR-3 polypeptide comprises amino acids encoded by exon 1b.

9. The polypeptide according to claim 1, where the KOR-3 polypeptide comprises mouse KOR-3C as depicted in Figure 4.

10. The polypeptide according to claim 9, where the KOR-3 polypeptide comprises amino acids encoded by exon 1c.

11. The polypeptide according to claim 1, where the KOR-3 polypeptide comprises mouse KOR-3E as depicted in Figure 5.

12. The polypeptide according to claim 11, where the KOR-3 polypeptide comprises amino acids encoded by exon 2a.

13. The polypeptide according to claim 1, where the KOR-3 polypeptide comprises rat KOR-3A as depicted in Figure 6.

14. The polypeptide according to claim 13, where the KOR-3 polypeptide comprises amino acids encoded by exon 1a.

15. The polypeptide according to claim 1, where the KOR-3 polypeptide comprises human KOR-3A as depicted in Figure 7.

16. The polypeptide according to claim 15, where the KOR-3 polypeptide comprises amino acids encoded by exon 1a.

17. The polypeptide according to claim 1, where the KOR-3 polypeptide comprises human KOR-3D as depicted in Figure 8.

18. The polypeptide according to claim 17, where the KOR-3 polypeptide comprises amino acids encoded by exon 1d.

19. The polypeptide according to claim 1 consisting of a heterodimeric or homodimeric composition.

20. The polypeptide, according to claim 1, where the homolog is a human homolog.

21. An isolated polynucleotide, or a complementary strand thereto that hybridizes under stringent conditions, comprising at least 15 consecutive nucleotides of the KOR-3 polynucleotide fragment depicted in Figures 2-8 where the polynucleotide is not the same as a polynucleotide derived from any known KOR-3 polynucleotide.

22. The polynucleotide according to claim 21, where the nucleotide fragment comprises at least 15 consecutive nucleotides of mouse KOR-3A depicted in Figure 9.

23. The polynucleotide according to claim 22, where the nucleotide fragment comprises bases exon 1a.

24. The polynucleotide according to claim 21, where the nucleotide fragment comprises at least 15 consecutive nucleotides of mouse KOR-3B depicted in Figure 10.

25. The polynucleotide according to claim 24, where the nucleotide fragment comprises exon 1b.

26. The polynucleotide according to claim 21, where the nucleotide fragment comprises at least 15 consecutive nucleotides of mouse KOR-3C as depicted in Figure 11.

27. The polynucleotide according to claim 26, where the nucleotide fragment comprises exon 1c.

28. The polynucleotide according to claim 21, where the nucleotide fragment comprises at least 15 consecutive nucleotides of mouse KOR-3E as depicted in Figure 12.

29. The polynucleotide according to claim 28, where the nucleotide fragment comprises exon 2a.

30. The polynucleotide according to claim 21, where the nucleotide fragment comprises at least 15 consecutive nucleotides of rat KOR-3A as depicted in Figure 13.

31. The polynucleotide according to claim 30, where the nucleotide fragment comprises exon 1a.

32. The polynucleotide according to claim 21, where the nucleotide fragment comprises at least 15 consecutive nucleotides of human KOR-3A as depicted in Figure 14.

33. The polynucleotide according to claim 32, where the nucleotide fragment comprises exon 1a.

34. The polynucleotide according to claim 21, where the nucleotide fragment comprises at least 15 consecutive nucleotides of human KOR-3D as depicted in Figure 15.

35. The polynucleotide according to claim 34, where the nucleotide fragment comprises exon 1d.

36. A polynucleotide, or a complementary strand thereto that hybridizes under stringent conditions, of at least 15 consecutive nucleotides encoding the isolated KOR-3 polypeptide.

37. The polynucleotide according to claim 36, where the KOR-3 polypeptide comprises mouse KOR-3A as depicted in Figure 2.

38. The polynucleotide according to claim 37, where the KOR-3 polypeptide comprises amino acids encoded by exon 1a.

39. The polynucleotide according to claim 36, where the KOR-3 polypeptide comprises mouse KOR-3B as depicted in Figure 3.

40. The polynucleotide according to claim 39, where the KOR-3 polypeptide comprises amino acids encoded by exon 1b.

41. The polynucleotide according to claim 36, where the KOR-3 polypeptide comprises mouse KOR-3C as depicted in Figure 4.

42. The polynucleotide according to claim 41, where the KOR-3 polypeptide comprises amino acids encoded by exon 1c.

43. The polynucleotide according to claim 36, where the KOR-3 polypeptide comprises mouse KOR-3E as depicted in Figure 5.

44. The polynucleotide according to claim 43, where the KOR-3 polypeptide comprises amino acids encoded by exon 2a.

45. The polynucleotide according to claim 36, where the KOR-3 polypeptide comprises rat KOR-3A as depicted in Figure 6.

46. The polynucleotide according to claim 45, where the KOR-3 polypeptide comprises amino acids encoded by exon 1a.

47. The polynucleotide according to claim 36, where the KOR-3 polypeptide comprises human KOR-3A as depicted in Figure 7.

48. The polynucleotide according to claim 47, where the KOR-3 polypeptide comprises amino acids encoded by exon 1a.

49. The polynucleotide according to claim 36, where the KOR-3 polypeptide comprises human KOR-3D as depicted in Figure 8.

50. The polynucleotide according to claim 49, where the KOR-3 polypeptide comprises amino acids encoded by exon 1d.

51. The nucleic acid of claim 21 or 36 contained in a vector molecule.

52. The nucleic acid of claim 21 or 36 contained in an expression vector and operably linked to a promoter element.

53. A method of screening compositions for opioid activity comprising the steps of

a) obtaining a control cell that does not express a recombinant opioid receptor;

b) obtaining a test cell that is the same as the control cell except that it expresses a recombinant opioid receptor selected from the group consisting of an KOR-3 splice variant polypeptide;

c) contacting the control cell and test cell with an amount of an opioid sufficient to exert a physiologic effect;

d) separately measuring the physiologic effect of the composition on the control cell and test cell; and

e) comparing the physiologic effect of the composition to the physiologic effect of the opioid, where determination of a physiologic effect of the composition is expressed relative to that of the opioid.

54. The method according to claim 53, where the composition is selected from the group consisting of synthetic combinatorial libraries of small molecule ligands, eukaryotic whole cell lysates or extracts, or media conditioned by cultured eukaryotic cells.

55. The method according to claim 53, where the opioid is selected from the group consisting of morphine, etorphine, levorphanol, nalbuphine, naloxone benzoylhydrazone, [D-Ala$^2$,MePhe$^4$,Gly(ol)$^5$]enkephalin (DAMGO), pentazocine, ethylketocyclazocine, and bremazocine.

56. The method according to claim 53, where the physiologic effect is measured by changes in the levels of neuroendocrine hormones.

57. The hormone according to claim 56, where the hormone is selected from the group consisting of prolactin, growth hormone, gonadotropin-releasing hormone, adrenocorticotropin, corticotropin-releasing factor, luteinizing hormone, follicle stimulating hormone, testosterone or cortisol.

58. The method according to claim 53, where the physiologic effect is measured by changes in the levels of neurotransmitters.

59. The neurotransmitter according to claim 58, where the neurotransmitter is acetylcholine or dopamine.

60. The method according to claim 53, where the homolog is a human homolog.

61. A method of screening compositions for opioid activity comprising the steps of

a) obtaining a control polypeptide that is not a recombinant opioid receptor;

b) obtaining a test polypeptide that is a recombinant opioid receptor selected from the group consisting of an KOR-3 splice variant polypeptide;

c) contacting a composition with the control polypeptide and the test polypeptide;

d) contacting the test polypeptide with an amount of an opioid sufficient to measurably bind the test polypeptide;

c) measuring the binding of the composition and the opioid; and

e) comparing test polypeptide binding of the composition to that of the opioid, where determination of binding of the composition is expressed relative to that of the opioid.

62. The method according to claim 61, where the composition is selected from the group consisting of synthetic combinatorial libraries of small molecule ligands, eukaryotic whole cell lysates or extracts, or media conditioned by cultured eukaryotic cells.

63. The method according to claim 61 where the homolog is a human homolog.

64. A method of screening compositions for differential opioid activity comprising the steps of

a) obtaining a first test polypeptide selected from the group consisting of an KOR-3 splice variant polypeptide, and contacting it with a composition;

b) obtaining a second test polypeptide selected from the group consisting of an KOR-3 splice variant polypeptide;

c) measuring the binding of the composition to the first and second test polypeptides; and

d) comparing the binding of the composition and the first test polypeptide to that of the second test polypeptide where differential activity is expressed as a ratio of the two binding affinities.

65. The method according to claim 64, where the composition is selected from the group consisting of synthetic combinatorial libraries of small molecule ligands, eukaryotic whole cell lysates or extracts, or media conditioned by cultured eukaryotic cells.

66. The method according to claim 64, where the homolog is a human homolog.

67. A non-human animal in which one or both endogenous KOR-3 alleles has been altered by homologous recombination with an exogenously introduced nucleic acid.

68. A non-human transgenic animal carrying a transgene comprising a nucleic acid that encodes a polypeptide selected from the group consisting of an KOR-3 splice variant polypeptide.

69. The transgenic animal according to claim 68, where the homolog is a human homolog.

70. A method for regulating morphine analgesia in a subject comprising altering the amount of KOR-3 polypeptide activity by

a) administering antigen binding fragments to a subject in an amount of and a duration sufficient to regulate morphine analgesia; or

b) administering agonists to a subject in an amount of and a duration sufficient to regulate morphine analgesia; or

c) administering antagonists to a subject in an amount of and a duration sufficient to regulate morphine analgesia; or

d) administering small molecule ligands to a subject in an amount of and a duration sufficient to regulate morphine analgesia; or

e) administering a DNA plasmid vector containing a nucleic acid encoding a polypeptide selected from the group consisting of an KOR-3 splice

variant polypeptide, thereby expressing an KOR-3 splice variant polypeptide in a subject in an amount of and a duration sufficient to regulate morphine analgesia; or

f) administering an antisense nucleic acid corresponding to a nucleic acid comprising a polypeptide encoding a polypeptide selected from the group consisting of an KOR-3 splice variant polypeptide, to a subject in an amount of and a duration sufficient to regulate morphine analgesia.

and wherein the antigen binding fragment, agonist, antagonist or small molecule ligand is directed to a polypeptide selected from the group consisting of an KOR-3 splice variant polypeptide.

71. The method according to claim 70, where the homolog is a human homolog.

72. A method for regulating body weight in a subject comprising altering the level of KOR-3 polypeptide activity by

a) administering antigen binding fragments to a subject in an amount of and a duration sufficient to regulate body weight; or

b) administering agonists to a subject in an amount of and a duration sufficient to regulate body weight; or

c) administering antagonists to a subject in an amount of and a duration sufficient to regulate body weight; or

d) administering small molecule ligands to a subject in an amount of and a duration sufficient to regulate body weight; or

e) administering a DNA plasmid vector containing a nucleic acid encoding a polypeptide selected from the group consisting of an KOR-3 splice variant polypeptide, thereby expressing an KOR-3 splice variant polypeptide in a subject in an amount of and a duration sufficient to regulate body weight; or

f) administering an antisense nucleic acid corresponding to a nucleic acid encoding a polypeptide selected from the group consisting of an KOR-3 splice variant polypeptide, to a subject in an amount of and a duration sufficient to regulate body weight.

and wherein the antigen binding fragment, agonist, antagonist or small molecule ligand is directed to a polypeptide selected from the group consisting of an KOR-3 splice variant polypeptide.

73. The method according to claim 72, where the homolog is a human homolog.

74. The method, according to claim 70 or 72, where the agonist is morphine, methadone, etorphine, levorphanol, fentanyl, sufentanil, [D-Ala$^2$,MePhe$^4$,Gly(ol)$^5$]enkephalin (DAMGO), butorphanol, naloxone, naltrexone, D-Phe-Cys-Tyr-D-Trp-Orn-Thr-Pen-Thr-$NH_2$ (CTOP), diprenorphine, β-funaltrexamine, naloxonazine, nalorphine, pentazocine, nalbuphine, benzoylhydrazone, bremazocine, ethylketocyclazocine, U50488, U69593 spiradoline, naltrindole, [D-Pen$^2$,D-Pen$^5$]enkephalin (DPDPE), [D-Ala$^2$,Glu$^4$]deltorphin, [D-Ser$^2$,Leu$^5$]enkephalin-Thr$^6$ (DSLET), Met-enkephalin, Leu-enkephalin, β-endorphin, dynorphin A, dynorphin B, or α-neoendorphin.

75. The method, according to claim 70 or 72, where the antagonist is morphine, methadone, etorphine, levorphanol, fentanyl, sufentanil, [D-Ala$^2$,MePhe$^4$,Gly(ol)$^5$]enkephalin (DAMGO), butorphanol, naloxone, naltrexone, D-Phe-Cys-Tyr-D-Trp-Orn-Thr-Pen-Thr-$NH_2$ (CTOP), diprenorphine, β-funaltrexamine, naloxonazine, nalorphine, pentazocine, nalbuphine, benzoylhydrazone, bremazocine, ethylketocyclazocine, U50488, U69593 spiradoline, naltrindole, [D-Pen$^2$,D-Pen$^5$]enkephalin (DPDPE), [D-Ala$^2$,Glu$^4$]deltorphin, [D-Ser$^2$,Leu$^5$]enkephalin-Thr$^6$ (DSLET), Met-enkephalin, Leu-enkephalin, β-endorphin, dynorphin A, dynorphin B, or α-neoendorphin.

76. A method for diagnosing an KOR-3 splice variant-associated pharmacological abnormality, comprising measuring the amount of variant activity or tissue distribution thereof in a subject and comparing that activity or tissue distribution to a control sample, wherein a difference in the amount of activity or tissue distribution correlates with the presence of a pharmacological defect.

77. The method according to claim 76, where the disorder is a heritable disorder.

78. A method for diagnosing an KOR-3 splice variant-associated disorder of the neuroendocrine system, comprising measuring the amount of variant activity or tissue distribution in a subject and comparing that activity or tissue distribution to a control sample, wherein a difference in the amount of activity or tissue distribution correlates with the presence of a defect within the neuroendocrine system.

79. The method according to claim 78 where the disorder is a heritable disorder.

80. A method for generating antigen binding fragments specific for a KOR-3 splice variant polypeptide.